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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,281	10/30/2003	Paul K. Wolber	10030355-1	3574

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AGILENT TECHNOLOGIES INC.
INTELLECTUAL PROPERTY ADMINISTRATION, LEGAL DEPT,
M/S DU404
P.O. BOX 7599
LOVELAND, CO 80537-0599

EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,281	WOLBER ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

This action is in response to papers filed 30 May 2006 in which claims 21 and 22 were amended, no claims were canceled, and no claims were added. All of the amendments have been thoroughly reviewed and entered.

1. The previous rejections under 35 U.S.C. 112, second paragraph, not reiterated below are withdrawn in view of Applicant's arguments.

2. The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of Applicant's arguments. Applicant's remaining arguments have been thoroughly reviewed and are addressed as needed following the rejections.

3. Claims 1-13 and 21-25 are under prosecution.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. 1.

Claim 3 is indefinite in the recitation "said amount" at the end of the claim. It is unclear whether "said amount" refers to "the amount" of claim 1 or "a relative amount" of claim 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by McGall (U.S. Patent No. 5,843,655, issued 1 December 1998).

Regarding claim 21, McGall teaches the method of detecting the presence of a nucleic acid analyte in a sample, said method comprising:

contacting a nucleic acid array, said array comprising a set of two or more nucleic acid depurination features (e.g., a nucleic acid array produced photolithographically [Figure 1] that includes at least one depurination probe feature of a depurination probe [e.g., depurinated oligonucleotides; Abstract, lines 4-5]) having a nucleic acid ligand that binds specifically to said nucleic acid analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur (e.g., samples are exposed to arrays under hybridization conditions [column 1, lines 30-37], and wherein depurinated oligonucleotides are subjected to cleavage and detection; column 13, lines 35-47); and

detecting the presence of binding complexes on the surface of said array to detect the presence of said nucleic acid analyte in said sample (column 1, lines 35-36; and wherein depurinated oligonucleotides are subjected to cleavage and detection; column 13, lines 35-47).

Regarding claim 23, McGall teaches the method of claim 21 further comprising transmitting a result from a reading of an array according to the method of claim 21 from a first location (e.g., the surface of the array) to a second location (e.g., a line scanner; column 12, lines 56-67).

Regarding claim 24, McGall teaches the method of claim 23 further comprising the second location is a remote location (e.g., a line scanner; column 12, lines 56-67).

Regarding claim 25, McGall teaches the method of claim 21 further comprising receiving a transmitted result of a reading of an array obtained from the method of claim 21 (e.g., images are stored in a computer; column 12, lines 56-67).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-13 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGall (U.S. Patent No. 5,843,655, issued 1 December 1998) in view of Weng et al (U.S. Patent No 6,691,042 B2, issued 10 February 2004).

Regarding claim 1, McGall teaches a method of detecting the presence of depurination reaction products on a surface of an in situ produced nucleic acid array, aid method comprising:

contacting an in situ produces nucleic acid array (e.g., a nucleic acid array produced photolithographically; Figure 1) that includes at least one depurination probe feature of a depurination probe (e.g., depurinated oligonucleotides [Abstract, lines 4-5] wherein the plural "oligonucleotides" is interpreted to mean more than one) with a sample that allows detection of the presence of depurination products on said surface (e.g., the array is exposed to a test condition that allows determination of the extent of depurination; column 2, lines 48-62). McGall also teaches that the arrays are used for

hybridization (column 1, lines 30-44; and wherein depurinated oligonucleotides are subjected to cleavage and detection; column 13, lines 35-47).

While McGall also teaches that test conditions comprise operating conditions (column 11, lines 35-41) and that operating conditions of the array includes hybridization of nucleic acids to the array (column 1, lines 30-44;], and wherein depurinated oligonucleotides are subjected to cleavage and detection; column 13, lines 35-47), McGall does not explicitly show hybridization as a test condition.

However, Weng et al teach a method of detecting the presence of nucleic acids (e.g., measuring expression levels of nucleic acids; column 8, lines 65-67) using microarrays (column 8, lines 60-64), wherein hybridization is used as a test condition (column 4, lines 58-67) with the added benefit of providing a method of controlling the quality of the microarray production process (column 5, lines 29-32).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall using hybridization as a test condition as taught by Weng et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in providing a method of controlling the quality of the microarray production process as explicitly taught by Weng et al (column 5, lines 29-32).

Regarding claim 2, the method of claim 1 is discussed above. Mc Gall also teaches that the method detects the amount of depurination products on said surface (column 2, lines 48-50).

Regarding claim 3, the method of claim 2 is discussed above. McGall also teaches the detection of a relative amount (column 7, lines 63-67).

Regarding claim 4, the method of claim 2 is discussed above. McGall also teaches the labeling of the target nucleic acid (column 11, lines 55-56).

Regarding claim 5, the method of claim 4 is discussed above. McGall also teaches fluorescent labels and signals (column 3, lines 24-31).

Regarding claim 6, the method of claim 5 is discussed above. McGall also teaches a fluorescent signal having an intensity inversely proportional to the amount of depurination products present (column 9, lines 65-67).

Regarding claim 7, the method of claim 1 is discussed above. McGall also teaches an array including two or more different depurination probe features each corresponding to a distinct depurination probe (e.g., the array has a plurality of nucleic acids; column 1, lines 30-44).

Regarding claim 8, the method of claim 1 is discussed above. McGall also teaches early and late depurination probe features (e.g., the depurination features occur at positions in the sequence relative to the surface; Figures 8 and 9).

Regarding claim 9, the method of claim 1 is discussed above. McGall also teaches arrays including two or more features whose synthesis was started at different times (areas on the surface are sequentially synthesized; column 9, lines 30-35).

Regarding claim 10, the method of claim 1 is discussed above. McGall also teaches a known deblock dose (e.g., selective deprotection and coupling cycles are repeated until the desired products are obtained [column 5, lines 2-25], the desired products requiring a known number of cycles).

Regarding claim 11, the method of claim 1 is discussed above. McGall also teaches the method further comprises evaluating the level of depurination that occurred during in situ fabrication of said array (column 2, lines 48-50).

Regarding claim 12, the method of claim 11 is discussed above. McGall also teaches the method is a method of evaluating the quality of an in situ nucleic acid array synthesis protocol (column 1, lines 7-9).

Regarding claim 13, the method of claim 12 is discussed above. McGall also teaches the method is employed to evaluate the quality of a plurality of nucleic acid arrays fabricated according to said protocol (e.g., arrays in different test areas on the substrate are independently evaluated; column 9, lines 38-49).

Regarding claim 22, McGall teaches the method of claim 21 of detecting the presence of a nucleic acid analyte in a sample, said method comprising:

contacting a nucleic acid array, said array comprising a set of two or more nucleic acid depurination features (e.g., a nucleic acid array produced photolithographically [Figure 1] that includes at least one depurination probe feature of a depurination probe [e.g., depurinated oligonucleotides; Abstract, lines 4-5]) having a nucleic acid ligand that binds specifically to said nucleic acid analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur (e.g., samples are exposed to arrays under hybridization conditions; column 1, lines 30-37); and

detecting the presence of binding complexes on the surface of said array to detect the presence of said nucleic acid analyte in said sample (column 1, lines 35-36).

While McGall also teaches that test conditions comprise operating conditions (column 11, lines 35-41) and that operating conditions of the array includes hybridization of nucleic acids to the array (column 1, lines 30-44), McGall does not explicitly show hybridization as a test condition.

However, Weng et al teach a method of detecting the presence of nucleic acids (e.g., measuring expression levels of nucleic acids; column 8, lines 65-67) using microarrays (column 8, lines 60-64), wherein hybridization is used as a test condition (column 4, lines 58-67) with the added benefit of providing a method of controlling the quality of the microarray production process (column 5, lines 29-32).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall using hybridization as a test condition as taught by Weng et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in providing a method of controlling the quality of the microarray production process as explicitly taught by Weng et al (column 5, lines 29-32).

Response to Arguments

Applicant's arguments filed 30 May 2006 (i.e., "the Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

1. Applicant argues on page 6 of the Remarks that that examination of Group II would not be burdensome because claim 14 has already been searched and examined. The argument is moot because the requirement for restriction has already been deemed proper and made **FINAL** in the Office Action dated 17 March 2006. In addition, examination of Group II would include the additional limitations set forth in remaining claims 15-20 of Group II, each of which has limitations **not present in the claims of Group I** (e.g., polyA, differing lengths, staggered start probes, etc.). A search of these additional limitations would therefore constitute a significant burden on the Office, and the restriction is therefore proper.

2. Applicant argues on page 7 of the Remarks that "a relative amount" are recited in claim 3 is not indefinite because a definition of "a relative amount" is provided in the Specification.

The rejection of "a relative amount" as indefinite is withdrawn. However, the limitation "said amount" is now rejected under 35 USC 112, second paragraph, because it is unclear whether "said amount" refers to "the amount" of claim 1 or "a relative amount" of claim 2.

3. Applicant argues on page 7 of the Remarks that the recitations of "early" and "late" in claim 8 are not indefinite because Figures 1 and 2, the description of Figures 1 and 2, and page 17, paragraph 3 of the Specification make it clear how Applicants are using the terms.

Figures 1 and 2 each provide "a depiction of representative" early and late probes "according to an embodiment of the subject invention." Use of the open language "a depiction" and "an embodiment" in the descriptions of Figure 1 and 2 clearly indicates that the Figures are indicative of one, but not all,

embodiments of the early and late probes. Figures 1 and 2 and their respective descriptions therefore lack the definitive embodiment of the early and late probes.

In addition, paragraph 3 of page 17 of the Specification merely states that the probes may be divided into the subgroups of early and late probes, and that the numbers of each type of probe may vary according to several broad ratios. As such, the cited paragraph only teaches two groups comprising variable numbers of probes. The paragraph does not provide an explicit definition to discriminate between the claimed early and late probes, and therefore lacks the definitive embodiment of the early and late probes.

The rejection of claim 8 under 35 USC 112, second paragraph is therefore withdrawn. The claim has been interpreted in the broadest reasonable interpretation consistent with the Specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]),

4. The arguments on page 8 of the Remarks regarding Church et al are moot in view of the withdrawn rejection.

5. Applicant argues on pages 8-9 of the Remarks that McGall does not teach the method of claim 21. Applicant argues on page 9 that the sections of column 1 cited are general background information that are not germane to McGall's invention.

However, the courts have stated "[A] prior art reference must be considered in its entirety, i.e., as a whole" *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983) (see MPEP 2141.02 [R-3] VI). The citations of column 1 of McGall do clearly indicate method steps using oligonucleotide arrays, included those of McGall, in hybridization methods. In addition, McGall clearly teaches hybridization of targets to the array as part of the method taught by McGall et al (e.g., depurinated oligonucleotides are subjected to cleavage and detection; column 13, lines 35-47).

Applicant acknowledges on page 9 of the Remarks that McGall test for depurination, but argues the McGall detects the amount of uncleaved oligonucleotides, and that this is not the same as forming a binding complex between a depurination probe and a target nucleic acid and detecting the amount of binding complexes.

However, the claim does not require the formation of a binding complex between a depurination probe and a target nucleic acid. Claim 21 is drawn to contacting an array comprising a set of two or more nucleic acid depurination features (claim 14), and that the array has a nucleic acid ligand that binds to the analyte. The claim does **not** require that the nucleic acid ligand be one of the depurination features. McGall teaches contacting a nucleic acid array, said array comprising a set of two or more nucleic acid depurination features (e.g., a nucleic acid array produced photolithographically [Figure 1] that includes at least one depurination probe feature of a depurination probe [i.e., the plural "oligonucleotides" indicates more that one depurinated oligonucleotide is present]; Abstract, lines 4-5]) having a nucleic acid ligand that binds specifically to said nucleic acid analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur (e.g., samples are exposed to arrays under hybridization conditions; column 13, lines 34-52).

Applicant also acknowledges of page 9 of the Remarks that McGall determines the amount of uncleaved oligonucleotides. As stated above, claim 21 requires the detection of binding complexes between the nucleic acid ligand on the array (i.e., an oligonucleotide on the array that is **not** required to be a depurination feature), and detecting the presence of binding complexes on the surface of said array to detect the presence of said nucleic acid analyte in said sample (e.g., hybridization is detected on the array using a CCD imaging system; column 13, lines 34-52). Therefore, McGall teaches each and every limitation of claim 21, and the claim is anticipated by McGall.

6. The remaining arguments on pages 9-10 of the Remarks regarding McGall et al in view of Church et al are moot in view of the withdrawn rejections.

Conclusion

1. No claim is allowed.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634